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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,567	11/14/2003	Paul Wentworth	1361.028US1	1768

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EXAMINER	
JUNG, UNSU	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/714,567	WENTWORTH ET AL.	
	Examiner	Art Unit	
	UNSU JUNG	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-13 and 15-44* is/are pending in the application.

4a) Of the above claim(s) *21-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-13 and 15-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Examiner for the current application has been changed from David J. Venci to Unsu Jung in Art Unit 1641. Any inquiry concerning this application should be directed to Unsu Jung, whose contact information is provided in the conclusion section of this Office Action.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on March 16, 2009 has been entered. The submission included amendments to claims 1, 3, 11, and 13.

Status of Claims

3. Claims 1-3, 5-13, and 15-44 are pending, claims 21-44 have been withdrawn from consideration, and claims 1-3, 5-13, and 15-20 are currently under consideration for patentability under 37 CFR 1.104.

Priority

4. This application was filed under 35 U.S.C. § 111(a) on November 14, 2003. This application is a continuation-in-part of U.S. Patent Application Serial No. 10/380,905 filed under 35 U.S.C. § 371 on December 19, 2003, and claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Application Serial No.'s 60/426,245, filed November 14, 2002, 60/235475, filed September 26, 2000, 60/232,702, filed September 15, 2000, and 60/315906, filed August 29, 2001.

Specification

5. The disclosure is objected to because of the following informalities:

Throughout the specification, reference to the conversion of "singlet oxygen" into "reactive oxygen species" appears repugnant to the art-recognized definition of "reactive oxygen species" because persons skilled in the art generally do not recognize "singlet oxygen" as a separate genus, but rather recognize that "singlet oxygen" belongs to the broader genus of "reactive oxygen species."
Furthermore:

> On p. 24, lines 27-28, the phrase "[t]he role of the newly discovered chemical potential of antibodies [to generate reactive oxygen species] *in vivo* is dependent on the availability of the key substrate $^1O_2$*" (paraphrasing mine) is not clear in view of p. 18, lines 4-5 phrase "the term 'reactive oxygen species' means antibody-generated oxygen species". The source of *in vivo* $^1O_2$* is not clear.

On p. 30, line 13, the phrase "[i]n the present invention, the minimum requirements are singlet oxygen, an antibody reagent…" (paraphrasing mine) is not clear in view of p. 18, lines 4-5 phrase "the term 'reactive oxygen species' means antibody-generated oxygen species". The source of *in vivo* $^1O_2$* is not clear.

Appropriate correction is required.

Rejections Withdrawn

6. The rejection of claims 1-3, 5-13, and 15-20 under 35 U.S.C. 112, second paragraph has been withdrawn in view of amended claims 1, 3, 11, and 13, and 22 in the reply filed on March 16, 2009.

7. The new matter rejection of claims 1-3, 5-13, and 15-20 under 35 U.S.C. 112, second paragraph has been withdrawn in view of amended claims 1, 3, 11, and 13, and 22 in the reply filed on March 16, 2009.

8. Applicant's arguments, see p15, filed on March 16, 2009, with respect to the rejection under 35 U.S.C. 102(b) as being anticipated by Hewitt et al. (Ann. Rhem. Dis., 1987, Vol. 46, pp866-874) have been fully considered and are persuasive. The rejection of claims 1, 2, 5, 7-12, 15 and 17-20 under 35 U.S.C. 102(b) as being anticipated by Hewitt et al. has been withdrawn.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Written Description

Claims 1-3, 5-13, and 15-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP stats that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention."

The claims lack adequate written description for the following reasons. The instant claims recite a method for detecting an immunological response in a mammal by detecting the presence of an oxidized chemical probe administered to the mammal. The claims therefore are broadly drawn to methods of detecting an immunological response in the mammal by detecting the presence of an oxidized chemical probe administered to the mammal.

Further, the current specification lacks guidance with regard to the detection of immunological response in a mammal by detecting the presence of oxidized chemical probe in a sample. Although the current specification discloses that reactive oxygen species includes antibody or neutrophil generated reactive oxygen species (p4, lines 27-28), the specification fails to demonstrate how reactive oxygen levels can serve as marker and/or indicator of immunological response. Palozza et al. (*Methods in Enzymology*, 1992, Vol. 213, pp.403-420, hereinafter "Palozza") discloses that oxygen radicals (reactive oxygen species) are involved in a variety of conditions including cancer, cataract, atherosclerosis, and the process of aging (p403, 5th paragraph). Therefore, the reactive oxygen species are not specific indicator of immunological response as reactive oxygen species are also associated with other conditions such as cancer, cataract, atherosclerosis, and the process of aging.

Since the method of instant claims for detecting an immunological response in a mammal by detecting the presence of an oxidized alkene-containing chemical probe administered to the mammal is not known in the prior art, the specification, in failing to disclose how the oxidized alkene-containing chemical probe can be used to assess the immunological response in a mammal, would not reasonably convey possession of the entire scope of the claimed invention to one of ordinary skill in the art.

Accordingly, it is deemed that the specification fails to provide adequate written description for detecting an immunological response in a mammal by detecting the presence of an oxidized alkene-containing chemical probe administered to the mammal and does not reasonably convey to one of ordinary skill in the art that the inventor(s), at

the time of the application was filed, had possession of the entire scope of the claimed invention.

11. Enablement

Claims 1-3, 5-13, and 15-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The nature of the invention is drawn to a method for detecting an immunological response in a mammal by detecting the presence of an oxidized chemical probe administered to the mammal. The claims therefore encompass methods of detecting an immunological response in the mammal by detecting the presence of an oxidized chemical probe administered to the mammal.

The current specification discloses *in vitro* detection of probes for "reactive oxygen species" which are *in vitro* oxidized by *in vitro* antibody-generated oxygen. Specifically, the specification teaches:

1. UV-irradiated antibody catalyzes formation of one or more Amplex® Red oxidants (see Fig. 3, □; see *also*, Fig. 7A; see *also*, Fig. 8, ●, Δ, □, ○; see *also*, Figs. 8B, 8C, 8E, 8F and 10B), tris carboxyethyl phosphine oxidants (see Figs. 12A, 12B and 12C, m/z = 265, 267), and indigo carmine oxidants (see Fig. 18B).

2. White light-irradiated hematoporphyrin catalyzes formation of one or more indigo carmine oxidants (see Fig. 19C), especially in the presence of an antibody electron donor (see Fig. 19 B).

3. UV-irradiated hematoporphyrin catalyzes formation of one or more Amplex® Red hydrogen peroxide products (see Fig. 5, ♦), especially in the presence of an antibody electron donor (see Fig. 5, ●).

The specification does not provide detection methods specific for administered probes for "reactive oxygen species", or specific for administered probes which are oxidized by *in vivo* antibody-generated oxygen. The specification provides no direction for performing a method commensurate in scope to the claimed invention. None of the analytical instruments and techniques described in the specification (see *generally*, Specification, p. 24, lines 9-13) applied to the claimed method for detecting administered probes for "reactive oxygen species", or for detecting administered probes which were oxidized by *in vivo* antibody-generated oxygen. The specification provides no working examples evidencing any of the aforementioned probes (*i.e.*, 10-acetyl-3,7-dihydroxyphenoxazine, tris carboxyethyl phosphine, indigo carmine) or any of the probes listed in claims 3 or 13 (*i.e.*, vinyl-benzoic acid, indigo carmine) being oxidized *in vivo* by antibody-generated oxygen.

Palozza suggests that *in vivo* administered alkene-containing chemical probes (carotenoids) cannot be detected as an oxidized form to indicate plasma or tissue levels of the chemical probes (p417, *Animal Studies*, *Direct Antioxidant Activity*). In addition, Hewitt et al. (*Ann. Rhem. Dis.*, 1987, Vol. 46, pp866-874, hereinafter “Hewitt”)

discovered that measurements of lipid peroxidation, diene conjugate and fluorescent IgG in exudates (see Figs. 2 and 3) fail to sensitively distinguish between control rats *versus* rats administered UV-irradiated antibodies, suggesting that these antibodies are not catalyzing formation of "reactive oxygen species" to create oxidized probes (*i.e.*, oxidized lipids, dienes and IgGs) to any significant level of detection. Therefore, the state of the art indicates that the oxidized levels of alkene-containing chemical probes cannot be used as an indicator of reactive oxygen species in a mammal as currently recited in instant claims.

Further, the current specification lacks guidance with regard to the detection of immunological response in a mammal by detecting the presence of oxidized chemical probe in a sample. Although the current specification discloses that reactive oxygen species includes antibody or neutrophil generated reactive oxygen species (p4, lines 27-28), the specification fails to demonstrate how reactive oxygen levels can serve as marker and/or indicator of immunological response. Palozza discloses that oxygen radicals (reactive oxygen species) are involved in a variety of conditions including cancer, cataract, atherosclerosis, and the process of aging (p403, 5th paragraph). Therefore, the reactive oxygen species are not specific indicator of immunological response as reactive oxygen species are also associated with other conditions such as cancer, cataract, atherosclerosis, and the process of aging.

In summary, the specification fails to teach that the claimed method steps of oxidized alkene-containing chemical probe can be detected after being administered in a mammal and that the presence of oxidized alkene-containing chemical probe can be

used to detect immunological response in a mammal. In particular, the specification fails to teach one of ordinary skill in the art how to detect immunological response in a mammal by detecting the presence of oxidized alkene-containing chemical probe since the specification fail to disclose any method steps for how to distinguish immunological response from other conditions such as cancer, cataract, atherosclerosis, and the process of aging, which are associated with reactive oxygen species. Consequently, the specification fails to teach one of ordinary skill in the art how to make and use the claimed invention without undue experimentation.

Response to Arguments

12. Enablement

Applicant's arguments filed on March 16, 2009 have been fully considered but they are not persuasive essentially for the reasons of record and arguments addressed herein.

Applicant's argument that the claimed invention does not recite detecting *in vivo* an oxidized product of the administered probe has been fully considered. Although it is acknowledged that the oxidized product is detected following the step of obtaining a sample from the mammal, the oxidation occurs *in vivo*. Palozza suggests that *in vivo* administered alkene-containing chemical probes (carotenoids) cannot be detected as an oxidized form to indicate plasma or tissue levels of the chemical probes (p417, *Animal Studies*, *Direct Antioxidant Activity*). In addition, Hewitt discovered that measurements of lipid peroxidation, diene conjugate and fluorescent IgG in exudates

(see Figs. 2 and 3) fail to sensitively distinguish between control rats *versus* rats administered UV-irradiated antibodies, suggesting that these antibodies are not catalyzing formation of "reactive oxygen species" to create oxidized probes (*i.e.*, oxidized lipids, dienes and IgGs) to any significant level of detection. Therefore, the state of the art indicates that the oxidized levels of alkene-containing chemical probes cannot be used as an indicator of reactive oxygen species in a mammal as currently recited in instant claims.

Applicant's argument that all the steps entailed by the claimed methods can be readily carried out in accordance with the subject disclosure and techniques well known in the art has been fully considered but is not found persuasive essentially for the reasons set forth in the current Office Action. As set forth above, Palozza suggests that *in vivo* administered alkene-containing chemical probes (carotenoids) cannot be detected as an oxidized form to indicate plasma or tissue levels of the chemical probes (p417, *Animal Studies*, *Direct Antioxidant Activity*). In addition, Hewitt discovered that measurements of lipid peroxidation, diene conjugate and fluorescent IgG in exudates (see Figs. 2 and 3) fail to sensitively distinguish between control rats *versus* rats administered UV-irradiated antibodies, suggesting that these antibodies are not catalyzing formation of "reactive oxygen species" to create oxidized probes (*i.e.*, oxidized lipids, dienes and IgGs) to any significant level of detection. Therefore, the state of the art indicates that the oxidized levels of alkene-containing chemical probes cannot be used as an indicator of reactive oxygen species in a mammal as currently recited in instant claims.

Further, the current specification lacks guidance with regard to the detection of immunological response in a mammal by detecting the presence of oxidized chemical probe in a sample. Although the current specification discloses that reactive oxygen species includes antibody or neutrophil generated reactive oxygen species (p4, lines 27-28), the specification fails to demonstrate how reactive oxygen levels can serve as marker and/or indicator of immunological response. Palozza discloses that oxygen radicals (reactive oxygen species) are involved in a variety of conditions including cancer, cataract, atherosclerosis, and the process of aging (p403, 5th paragraph). Therefore, the reactive oxygen species are not specific indicator of immunological response as reactive oxygen species are also associated with other conditions such as cancer, cataract, atherosclerosis, and the process of aging.

In view of the foregoing the rejection of claims 1-3, 5-13, and 15-20 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement has been maintained.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to UNSU JUNG whose telephone number is (571)272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Unsu Jung/
Unsu Jung
Primary Examiner
Art Unit 1641